



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH

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DATE: May 5, 2022

TO: Michael M. Gottesman, M.D.  
Deputy Director for Intramural Research, NIH

FROM: Director  
Division of Compliance Oversight, OLAW

SUBJECT: Animal Welfare Investigation (NIDA #10-22) - Animal Welfare Assurance  
A4149-01 [Case 16N]

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 27, 2022 memo regarding an incident of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the National Institute on Drug Abuse (NIDA). According to the information provided, OLAW understands that on March 9, 2022, it was determined that eight mice that had undergone intracranial injection had not received the required analgesic and had been kept past the experimental endpoint. Also, the surgeon was not approved to perform procedures on the protocol and had known that the procedure was not approved on the particular protocol. The surgeon admitted to performing thirty-eight such surgeries from November 2021 to March 1, 2022. The surgeon confirmed that he did not use a post-operative analgesic for any of the animals receiving surgery from sometime in January 2022 until March 2022. It was determined that the protocol deviations occurred with explicit intent by the surgeon to knowingly deviate from the protocol. Moreover, there was flagrant disregard for ACUC regulations and for the health and welfare of the animals involved. The violations occurred for many weeks and remained unchecked because of poor communication, faulty record keeping, and apparent efforts by the surgeon to hide any evidence of his activities.

The ACUC voted to adopt the following measures:

- 1) *Suspension of the primary surgeon.* The ACUC approved that this individual should not be allowed to perform any animal work at NIDA IRP. The individual's card access to the animal facility was revoked.
- 2) *Retraining of PI and lab personnel.* The PI and all personnel listed on the ASPs are to be retrained. Retraining will include completion of the full PI/animal user courses and surgeon's quiz for listed personnel.
- 3) *Improved oversight of lab communications and records.* The PI is to coordinate, together with the Branch Chief, a strategy for regular meetings within the lab that will focus on communication, proper record keeping practices, and a regular discussion of any animal health concerns, analgesic supply issues, etc.

- 4) *Suspension of animal research until retraining is complete.* The ACUC approved that all animal work on all protocols in the lab be suspended until all retraining is completed, and the Branch Chief ascertains that a sound strategy for improving lab communication is in place. At this time, the ACUC Chair and at least one other ACUC member will actively review all protocols with the PI and the entire lab, in order to ensure that all personnel are fully apprised of their respective roles and responsibilities on each protocol. After this review, research activities may resume.

The actions taken to resolve the issues and prevent recurrence were appropriate and accepted by OLAW. The NIDA ACUC is to be commended for their strong stance in favor of animal welfare and scientific integrity. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

**Brent C. Morse** – Digitally signed by Brent C.  
Morse -S  
S Date: 2022.05.05 15:50:50 -04'00'

Brent C. Morse, DVM, DACLAM  
Director  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare

cc: Dr. Stephen Denny  
Dr. Richard Wyatt  
Dr. Hoffman, NIDA ACUC Chair



**TO:** Dr. Michael Gottesman, Deputy Director for Intramural Research  
**FROM:** Alexander F. Hoffman, Chair, NIDA Animal Care and Use Committee  
**DATE:** 4/20/2022  
**SUBJECT:** Reportable incident on protocol non-compliance

The National Institute on Drug Abuse Intramural Research Program, in accordance with Assurance A4149-01 and PHS Policy IV.F.3., reports the following incident of protocol non-compliance involving improper surgical procedures in a protocol entitled "Striatal dopamine receptor heteromers as targets for drug development in Parkinson's disease and L-dopa-induced dyskinesia." A summary of the incident, major findings, and proposed remedies are described below.

**Summary of incident:** On 3/9/2022, during a routine walkthrough of the animal housing rooms, the ACUC Chair noted that 8 individually housed mice had post-operative cage cards that did not indicate the use of an analgesic. Animals had visible sutures on the skin overlying the skull and 'intracranial injection' was indicated on the cage cards. Surgery had been performed between 1-3 weeks prior to the date on which animals were discovered. A review of the protocol determined the following: (1) the listed surgeon the cage card was not approved on the ASP; (2) the protocol stipulated that ketoprofen was to be given following surgery; (3) the protocol stipulated that all surgical animals would be euthanized for their experimental endpoint within 48 hours after surgery. The ACUC Chair immediately communicated this concern to the NIH Office of Animal Care and Use, and appointed an ACUC subcommittee on 3/11/2022 to further investigate this incident.

#### **(1) Findings of the subcommittee**

The subcommittee presented its findings to the fully convened ACUC on 4/14/2022.

From their careful review of documentation as well as statements obtained from all individuals in the laboratory, the subcommittee found the following:

- *The surgeon did not receive final approval on the protocol owing to an administrative error. Although the lab had submitted an amendment and believed in good faith that the surgeon had been approved, an administrative error led to the PI not receiving the final assurance documentation.*

- *The surgeries performed, indicated as “intracranial injection, were not approved on the protocol.* The surgeon freely admitted that he performed the procedure consisting of direct intracranial injection, with full knowledge that the procedure was not approved on the protocol. It was further recognized that the surgeon took the sole initiative and responsibility to perform the surgeries, and no other lab members had any knowledge or involvement with his actions. The surgeon admitted to performing thirty eight such surgeries from November 2021 to March 1<sup>st</sup> 2022. The surgeon, as well as the PI and the surgeon’s direct supervisor, claimed that these were dye injections designed to evaluate optimal injection sites/probe placements for future experiments. The specific procedures performed on the animals could not be verified, as the PI requested that the 8 animals be euthanized.
- *No post-operative analgesics were given to an estimate of at least 12 animals.* The protocol requires the use of post-surgical analgesics, but none was administered nor recorded. The surgeon confirmed that he did not use a post-operative analgesic for any of the animals receiving surgery from sometime in January 2022 until March 2022. The surgeon claimed the reason for failure to administer analgesics was that the laboratory stock of the agents was expired in January 2022. Other members of the laboratory confirmed their use of post-operative analgesics for other surgeries during that same period of time.
- *At least 8 animals were kept for over 4 weeks post-operatively, beyond the approved disposition of 2-3 days post surgery, as outlined in the protocol.* The surgeon claimed that he kept the animals for longer than the approved time because he was testing a procedure that would be used in a future protocol, which dictated a longer post-surgery survival time. These statements are inconsistent with his claim that the animals were to be used for histological verification using dye injections, because such animals would not need to be kept for several weeks after injections.
- *Sutures were not removed on 4 animals past 2 weeks after surgery.*

Based on these findings, it is clear that the failure to follow procedures as described in the protocol represent a reportable animal welfare incident under OLAW Guidelines.

## **(2) Causes of Violations**

From the information obtained by the committee, it was determined that the protocol deviations occurred with explicit intent by the surgeon to knowingly deviate from the protocol. Moreover, there was flagrant disregard for ACUC regulations and for the health and welfare of the animals involved. The violations occurred for many weeks and remained unchecked because of poor communication, faulty record keeping, and apparent efforts by the surgeon to hide any evidence of his activities.

## **(3) ACUC Vote on Resolutions proposed by the subcommittee**



The subcommittee proposed several suggestions to mitigate against future violations, and the ACUC voted to adopt the following measures on 4/14/2022:

- 1) *Suspension of the primary surgeon.* Based on the surgeon's own admittance of knowingly violating the protocol without justification other than his own interest, his general demeanor of obstinance and defiance towards the sub-committee and ACUC requirements, his lack of regret or apology, and his generally dismissive attitude towards the consequences of his actions, the committee recommended, and the ACUC approved, that this individual should not be allowed to perform any animal work at NIDA IRP. The individual's card access to the animal facility was revoked as a precautionary measure. All members of the lab were informed of this suspension and were instructed to immediately report any suspected violation to the ACUC. Although such steps are unusual, the ACUC felt strongly that re-training this individual alone was not likely to mitigate against this particular individual's clear willingness to violate protocols.
- 2) *Retraining of PI and lab personnel.* Considering the failure, and apparent complicity of several laboratory members, to consider animal health and welfare as an utmost priority, failure to give proper training and/or supervision regarding animal welfare and proper adherence to the approved ASP, the sub-committee recommended, and the ACUC approved, that both the PI and all personnel listed on the ASPs be retrained. Retraining will include completion of the full PI/animal user courses and surgeon's quiz for listed personnel.
- 3) *Improved oversight of lab communications and records.* Given the poor record-keeping and communication issues within the lab, the subcommittee recommended, and the ACUC approved, that the PI coordinate, together with the Branch Chief, a strategy for more regular meetings within the lab that will focus on communication, proper record keeping practices, and a regular discussion of any animal health concerns, analgesic supply issues, etc. The PI and lab were provided with several NIH-based resources on best record-keeping practices.
- 4) *Suspension of animal research until retraining is complete.* The subcommittee recommended, and the ACUC approved, that all animal work on all protocols in the lab be suspended until all retraining is completed, and the Branch Chief ascertains that a sound strategy for improving lab communication is in place. At this time, the ACUC Chair and at least one other ACUC member will actively review all protocols with the PI and the entire lab, in order to ensure that all personnel are fully apprised of their respective roles and responsibilities on each protocol. After this review, research activities may resume.

### **Concluding statement**

The subcommittee found that a reportable animal welfare incident involving failure to adhere to the protocol did occur. The subcommittee and ACUC felt that this incident was largely the result of one individual's willingness to violate the protocol without any regard to regulations, animal welfare, or potential consequences. It is expected that the suspension of this individual from all animal work will prevent future recurrences. Nevertheless, it was also clear that poor record-keeping and communication played a major role in exacerbating the situation and allowing it to continue. The ACUC determined that such practices could be detrimental to the health and welfare of all animals involved in ongoing studies within this laboratory. Therefore, the recommended suspension of all research activities will allow the PI and staff to retrain and adjust their laboratory practices to improve their animal welfare oversight and responsibilities.

The NIDA IRP ACUC is committed to the highest animal welfare standards, and appreciates the support of OLAW in this regard. Should you have any additional questions or concerns regarding this report, please do not hesitate to contact me.

Sincerely,

(b) (6)

Alex Hoffman, Ph.D.

***Chair***

***NIDA IRP Animal Care and Use Committee***



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health  
Bethesda, Maryland 20892

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April 27, 2022

TO: Brent C. Morse, D.V.M.  
Director, Division of Compliance Oversight  
Office of Laboratory Animal Welfare

FROM: Deputy Director for Intramural Research, NIH

SUBJECT: Animal Welfare Investigations - Assurance D16-00602 (NIDA 10-22)

This correspondence conveys the results of an animal incident investigation by the NIH National Institute on Drug Abuse ACUC in accordance with Assurance D16-00602 and PHS Policy IV.F.3. The incident involved failure to conduct surgical procedures on mice as outlined in the corresponding ACUC-approved animal study proposal.

The event was first reported to the NIH Office of Animal Care and Use by the ACUC Chairman on March 9, 2022.

Please contact me or Dr. Stephen Denny, Director, Office of Animal Care and Use, if additional information or clarifications are required.

Michael M.  
Gottesman -S

Digitally signed by Michael M.  
Gottesman -S  
Date: 2022.04.28 09:10:07 -0400

Michael M. Gottesman, M.D.

Attachment

cc: Dr. Wyatt  
Dr. Hoffman  
Dr. Denny

**Wolff, Axel (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Friday, April 29, 2022 7:32 AM  
**To:** Denny, Stephen (NIH/OD) [E]  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: D16-00602 NIH Animal Incident Report (NIDA 10-22))

Thank you for this report, Dr. Denny. We will send a response shortly.

Axel Wolff, M.S., D.V.M.  
Deputy Director, OLAW

**From:** Denny, Stephen (NIH/OD) [E] <stephen.denny@nih.gov>  
**Sent:** Thursday, April 28, 2022 10:46 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Subject:** D16-00602 NIH Animal Incident Report (NIDA 10-22))

Dear OLAW/DCO,

The attached documents from the NIH Institutional Official and the NIH National Institute on Drug Abuse (NIDA) ACUC address an animal incident involving the failure of a research team to follow surgical activities and ACUC policies as outlined in the ACUC-approved Animal Study Proposal.. The event was first reported to the NIH Office of Animal Care and Use by the NIDA ACUC Chairman on March 9, 2022.

If you have any questions please contact me via email or at the phone number listed below. Thank you, Steve

STEPHEN DENNY, DVM, MS, DACLAM, DACVPM | Director, Office of Animal Care and Use | NIH Bethesda Campus, Building 31/Room B1C37 |  
Phone: (301) 435-2188 | **NIH . . . Turning Discovery Into Health** |